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In re application of: Khosravi, et al.	§	
Serial No.: Continuation of 09/484,903	§	Group Art Unit: 1642
Filed: Herewith	§	Examiner: Nickol, G.
For: INSULIN-LIKE GROWTH FACTOR SYSTEM AND CANCER	§	

PRELIMINARY AMENDMENT

Box New Application
Assistant Commissioner For Patents
Washington, DC 20231

Prior to the initial examination of the above-referenced application please enter the following changes:

In the Specification:

On page 1, after the Title, please add the following:

- - Cross-reference to Related Applications

This application is a continuation of application Serial No. 09/484,903, filed on January 18, 2000, now U.S. Patent No. _____. --

In the Claims:

Add the following new claims 17-55, and cancel claims 1-16 without prejudice or disclaimer:

- - 17. (New) A diagnostic method comprising:

collecting a body fluid from an individual;

measuring an insulin-like growth factor binding protein (IGFBP) concentration;

measuring a tumor marker concentration;

and calculating an indicator ratio based upon the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign disorders and cancer.

18. (New) The diagnostic method of claim 17 further comprising measuring an insulin-like growth factor (IGF) concentration, wherein the indicator ratio is based upon at least two of the measured concentrations.

19. (New) The diagnostic method of claim 18 wherein the IGF is IGF-I or IGF-II.

20. (New) The diagnostic method of claim 17 wherein the IGFBP is IGFBP-1, IGFBP-2, IGFBP-3, IGFBP-4, IGFBP-5, IGFBP-6, IGFBP-rP-1, IGFBP-rP-2, IGFBP-rP-3, IGFBP-rP-4, IGFBP-rP-5, IGFBP-rP-6, IGFBP-rP-7, IGFBP-rP-8, IGFBP-rP-9, or IGFBP protease.

21. (New) The diagnostic method of claim 17 wherein the IGFBP is total IGFBP-3 or intact IGFBP-3.

22. (New) The diagnostic method of claim 17 wherein the tumor marker is PSA, kallikrein, S-100 protein, C219, GCDFP-15/gp17, riboflavin carrier protein, vitamin carrier proteins, human chorionic gonadotropin, alpha-fetoprotein, lactate dehydrogenase, cytokeratin 19 fragment, CYFRA 21-1, carbohydrate antigen 19.9, macrophage-colony stimulating factor, abnormal prothrombin PIVKA-II, tissue polypeptide antigen, carcinoembroyonic antigen, cancer antigen 125, CA72-4, CA15-3, squamous cell antigen, neuron specific enolase, focal adhesion kinase, soluble CD44(sCD44), soluble CD30(sCD30), tissue polypeptide specific antigen (TPSA), total alkaline phosphate (T-ALP), urinary Dpd/creatinine (Cre) ratios, bone specific alkaline phosphatase (B-ALP), N-acetylneuraminic (Neu5Ac), vascular endothelial growth factor (VEGF), glutathione peroxidase, melanoma antigen (MAGE), mesothelin and megakaryocyte potentiating factor (MPF), cyclin-dependent kinase inhibitor p27 (Kip1), PGP9.5, proliferating cell nuclear antigen (PCNA), Cyclin D1, epidermal Growth Factor (EGF), transforming growth factor alpha (TGF alpha), estrogen receptor-related protein (ERRP), multidrug resistance marker (MDRM), protein kinase C (PKC), Gs alpha, inhibin, cathepsin D, H19, the steroid hormones, p53, and cytokines or interleukins.

23. (New) The diagnostic method of claim 17 wherein the tumor marker is PSA.

24. (New) The diagnostic method of claim 17 wherein the tumor marker is kallikrein.

25. (New) A diagnostic method comprising:

collecting a body fluid from an individual;

measuring an insulin-like growth factor binding protein (IGFBP) concentration;

measuring a growth factor concentration;

measuring a tumor marker concentration;

and calculating an indicator ratio based upon at least two of the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign disorders and cancer.

26. (New) The diagnostic method of claim 25 wherein the growth factor is IGF-I, IGF-II, GH, GHBP, GH receptor, IGF receptor, IGF proteases, ALS, IGF receptor antagonists or GH receptor antagonists.

27. (New) The diagnostic method of claim 25 wherein the IGFBP is IGFBP-1, IGFBP-2, IGFBP-3, IGFBP-4, IGFBP-5, IGFBP-6, IGFBP-rP-1, IGFBP-rP-2, IGFBP-rP-3, IGFBP-rP-4, IGFBP-rP-5, IGFBP-rP-6, IGFBP-rP-7, IGFBP-rP-8, IGFBP-rP-9, or IGFBP protease.

28. (New) The diagnostic method of claim 25 wherein the IGFBP is total IGFBP-3 or intact IGFBP-3.

29. (New) The diagnostic method of claim 25 wherein the tumor marker is PSA, kallikrein, S-100 protein, C219, GCDFP-15/gp17, riboflavin carrier protein, vitamin carrier proteins, human chorionic gonadotropin, alpha-fetoprotein, lactate dehydrogenase, cytokeratin 19 fragment, CYFRA 21-1, carbohydrate antigen 19.9, macrophage-colony stimulating factor, abnormal prothrombin PIVKA-II, tissue polypeptide antigen, carcinoembroyonic antigen, cancer antigen 125, CA72-4, CA15-3, squamous cell antigen, neuron specific enolase, focal adhesion kinase, soluble CD44(sCD44), soluble CD30(sCD30), tissue polypeptide specific antigen (TPSA), total alkaline phosphate (T-ALP), urinary Dpd/creatinine (Cre) ratios, bone specific alkaline phosphatase (B-ALP), N-acetylneuraminic (Neu5Ac), vascular endothelial growth factor (VEGF), glutathione peroxidase, melanoma antigen (MAGE), mesothelin and megakaryocyte potentiating factor (MPF), cyclin-dependent kinase inhibitor p27 (Kip1), PGP9.5, proliferating cell nuclear antigen (PCNA), Cyclin D1, epidermal Growth Factor (EGF), transforming growth factor alpha (TGF alpha), estrogen receptor-related protein (ERRP), multidrug resistance marker (MDRM), protein kinase C (PKC), Gs alpha, inhibin, cathepsin D, H19, the steroid hormones, p53, and cytokines or interleukins.

30. (New) The diagnostic method of claim 25 wherein the tumor marker is PSA.

31. (New) The diagnostic method of claim 25 wherein the tumor marker is kallikrein.

32. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a prostate specific antigen (PSA) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio based upon the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and prostate cancer.

33. (New) The diagnostic method of claim 32 wherein the IGFBP is total IGFBP-3 or intact IGFBP-3.

34. (New) The diagnostic method of claim 33 wherein the indicator ratio is (intact IGFBP-3/total IGFBP-3)/PSA.

35. (New) The diagnostic method of claim 33 wherein the indicator ratio is intact IGFBP-3/PSA.

36. (New) The diagnostic method of claim 33 wherein the indicator ratio is intact IGFBP-3.

37. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a prostate specific antigen (PSA) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio of (intact IGFBP-3/total IGFBP-3)/PSA based upon the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and prostate cancer.

38. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a prostate specific antigen (PSA) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio of intact IGFBP-3/PSA based upon the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and

prostate cancer.

39. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a prostate specific antigen (PSA) concentration;

measuring an insulin-like growth factor I (IGF-I) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio of (IGF-I/intact IGFBP-3/total IGFBP-3)/PSA based upon the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and prostate cancer.

40. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a prostate specific antigen (PSA) concentration;

measuring an insulin-like growth factor I (IGF-I) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio based upon at least two of the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and prostate cancer.

41. (New) A diagnostic method for discriminating between benign prostate disorders and prostate cancer in an individual, comprising:

collecting a body fluid from the individual;

measuring a kallikrein concentration;

measuring an insulin-like growth factor I (IGF-I) concentration;

measuring an insulin-like growth factor binding protein 3 (IGFBP-3) concentration;

and calculating an indicator ratio based upon at least two of the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign prostate disorders and prostate cancer.

42. (New) A diagnostic method comprising:

collecting a body fluid from an individual;

measuring a tumor marker concentration;

measuring a concentration selected from the group of insulin-like growth factor I (IGF-I) and insulin-like growth factor binding protein 3 (IGFBP-3);

and calculating an indicator ratio based upon at least two of the measured concentrations, wherein the indicator ratio provides a means for discriminating between benign disorders and prostate cancer.

43. (New) The diagnostic method of claim 42 wherein the tumor marker is PSA.

44. (New) The diagnostic method of claim 43 wherein the indicator ratio is IGF-I/PSA.

45. (New) The diagnostic method of claim 43 wherein the indicator ratio is Intact IGFBP-3/PSA.

46. (New) The diagnostic method of claim 43 wherein the indicator ratio is (IGF-I/total IGFBP-3/total IGFBP-3)/PSA.

47. (New) The diagnostic method of claim 43 wherein the indicator ratio is(IGF-I + Intact IGFBP-3)/PSA.

48. (New) The diagnostic method of claim 42 wherein the indicator ratio is Intact IGFBP-3.

49. (New) The diagnostic method of claim 42 wherein the tumor marker is kallikrein.

50. (New) The diagnostic method of claim 49 wherein the indicator ratio is IGF/kallikrein.

51. (New) The diagnostic method of claim 49 wherein the indicator ratio is IGFBP/kallikrein.

52. (New) The diagnostic method of claim 49 wherein the indicator ratio is IGF/IGFBP/kallikrein.

53. (New) The diagnostic method of claim 49 wherein the indicator ratio is (Intact IGFBP/total IGFBP)/kallikrein.

54. (New) The diagnostic method of claim 49 wherein the indicator ratio is (IGF + IGFBP)/kallikrein.

55. (New) The diagnostic method of claim 42 wherein the tumor marker is S-100 protein, C219, GCDFP-15/gp17, riboflavin carrier protein, vitamin carrier proteins, human chorionic gonadotropin, alpha-fetoprotein, lactate dehydrogenase, cytokeratin 19 fragment, CYFRA 21-1, carbohydrate antigen 19.9, macrophage-colony stimulating factor, abnormal prothrombin PIVKA-II, tissue polypeptide antigen, carcinoembroyonic antigen, cancer antigen 125, CA72-4, CA15-3, squamous cell antigen, neuron specific enolase, focal adhesion kinase, soluble CD44(sCD44), soluble CD30(sCD30), tissue polypeptide specific antigen (TPSA), total alkaline phosphate (T-ALP), urinary Dpd/creatinine (Cre) ratios, bone specific alkaline phosphatase (B-ALP), N-acetylneuraminic (Neu5Ac), vascular endothelial growth factor (VEGF), glutathione peroxidase, melanoma antigen (MAGE), mesothelin and megakaryocyte potentiating factor (MPF), cyclin-dependent kinase inhibitor p27 (Kip1), PGP9.5, proliferating cell nuclear antigen (PCNA), Cyclin D1, epidermal Growth Factor (EGF), transforming growth factor alpha (TGF alpha), estrogen receptor-related protein (ERRP), multidrug resistance marker (MDRM), protein kinase C (PKC), Gs alpha, inhibin, cathepsin D, H19, the steroid hormones, p53, and cytokines or interleukins. - -

Remarks

This application is a continuation of U.S. Serial No. 09/484,903.

Claims 17-55 have been added to claim an invention the Applicants' wish to protect. Claims 1-16 have been canceled.

Should the Examiner have any questions or comments, the Examiner is invited to telephone the undersigned at the number listed below.

Respectfully submitted,

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